CHAPTER 3

Results

3.1 Baseline characteristics of HIV-1 infected infants.

Three hundred twenty-five HIV-1 infected infants diagnosed during the period of year 2007 to year 2014 at the Faculty of Associated Medical Sciences (AMS), Chiang Mai University were enrolled. There were 297 available DBS of HIV infected infants were available for HIV proviral extraction, *pol* region amplification and nucleotide sequence determination. Only 287 (96.6%) DBS were successfully determined, while 10 (3.4%) were unable to be amplified any region. Among the 287 DBS, RT region were amplified in 275 (95.5%) DBS and PR region were amplified in 244 (84.7%) DBS and all of these were able to be sequenced. All available baseline characteristics and demographic data were collected. The data were shown in overall and according to different region of *pol* gene sequences (Table 3.1).

Of the total 287 samples, 131 (45.6%) were male and 156 (54.4%) female. The median age was 2.9 months (IQR=2.0-4.6). The most infants were born during July 2007 to August 2010 (141(49.1%) infants). There were 134 (46.7%) infants who born in the period September 2010 to August 2014. Eleven infants were born during September 2014 to December 2014. There were 53 (18.5%) infants that had clinical signs of HIV infection such as an influenza-like illness, swollen lymph nodes, weight loss, fever, diarrhea, and cough, whereas 208 (72.5%) had no signs of HIV infection and 26 (9.1%) infants had no available data.

Among 287 infants, 238 (82.9%) infants had been exposed to maternal and/or infant PMTCT. In 238 PMTCT-exposed infants, there were 171 (71.8%) infants who exposed maternal ARVs and 231 (97.1%) infants who exposed infant ARVs for prophylaxis. Forty-five (15.7%) infants had no recorded PMTCT exposures. The remaining 4 (1.4%) had no available PMTCT-exposed data.

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In case of infant prophylaxis 231 (80.5%) infants who received prophylaxis, while 48 (16.7%) infants were not received prophylaxis and 8 infants had no available data.There were 87 (41.1%) infants who received only AZT (for 27.0 days in average), 3 (1.0%) infants who received only single-dose NVP, 103 (57.0%) were received both AZT (for 26.0 days in average) and single-dose NVP, 27 (9.4%) infants were received AZT, NVP and 3TC (for 32.5, 26.6, and 31.8 days in average), 1 (0.3%) infant was received NVP, 3TC and d4T (duration data had no available) and 10 (3.5%) infants had history of ARV prophylaxis but had no available drug type data.

In maternal ARV-experienced data, there were 171 (59.6%) infants whose mothers received ARVs for PMTCT. Fifty-five (19.2%) infants whose mothers received only AZT during pregnancy at 198.3 days of gestational age in average, while 43 (15.0%) infants received AZT during pregnancy and sdNVP at delivery in199.0/236.6 days of gestational age in average, 66 (23.0%) infants were born to mothers who were on HAART during pregnancy at 168.3 days of gestational age in average, 104 (36.2%) infants were born to mothers who were not received ARV for MTCT prophylaxis and 8 (2.8%) infants had no available data.

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Table 3.1 The characteristics and demographic of HIV-infected infants in this study.

Characteristics	All (%) (n=287)	Number with sequenced RT (%), (n=275)	Number with sequenced PR (%), (n=244)
Age at sampling (months), median (IQR)	**2.9(2.0-4.6)**	**2.9(2.0-4.6)**	**3.0(2.1-4.7)**
Birth year/month			
2006/01- 2010/08	141(49.1)	133(48.4)	124(50.8)
2010/09 - 2014/08	134(46.7)	131(47.6)	110(45.08)
≥ 2014/09	11(3.8)	10(3.6)	9(3.7)
Missing data	1(0.3)	1(0.4)	1(0.4)
Gender			
Female	156(54.4)	150(54.5)	128(52.5)
Male	131(45.6)	125(45.5)	116(47.5)
Signs of infection			
No	208(72.5)	199(72.4)	177(72.5)
Yes	53(18.5)	52(18.91)	45(18.4)
Missing data	26(9.1)	24(8.7)	22(9.0)
Infant ARV prophylaxis	**Average time on ARVs (days)**	**Average time on ARVs (days)**	**Average time on ARVs (days)**
No	48(16.7)	48(17.5)	38(15.6)
Yes	231(80.5)	220(80.0)	198(81.1)

Table 3.1 (Continued)

Characteristics	All (%) (n=287)		Number with sequenced RT (%), (n=275)		Number with sequenced PR (%), (n=244)	
Missing data	8(2.8)		7(2.5)		8(3.3)	
AZT	87(30.3)	27.0	83(30.2)	27.1	74(30.3)	28.0
sdNVP	3(1.0)	after birth	3(1.1)	after birth	3(1.2)	after birth
AZT/sdNVP	10(35.9)	26.0/after birth	98(35.6)	26.1/after birth	90(36.9)	26.9/after birth
AZT/NVP/3TC	27(9.4)	32.5/26.6/31.8	27(9.8)	32.6/26.6/31.8	22 (9.0)	32.7/27.2/31.7
NVP/3TC/d4T	1(0.3)	NA	1(0.4)	NA	1(0.4)	NA
Missing drug data	10(3.5)		8(2.9)		8(3.3)	
Maternal ARV prophylaxis		**Gestational age at ARV initiation (in average days)**		**Gestational age at ARV initiation (in average days)**		**Gestational age at ARV initiation (in average day)**
No	104(36.2)		101(36.7)		90(36.9)	
Yes	171(59.6)		162(58.9)		142(58.2)	
Missing data	12(4.2)		12(4.4)		12(4.9)	
AZT	55(19.2)	198.3	50(18.2)	198.2	46(18.9)	199.2
AZT/sdNVP	43(15.0)	199.0/236.6	43(15.6)	199.0/236.6	38(15.6)	199.4/233.7
HAART	66(23.0)	168.3	62(22.5)	170.9	53(21.7)	172.8
Missing drug data	7(2.4)		7(2.5)		5(2.0)	

NA, not available data

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3.2 Amplification of HIV reverse transcriptase and protease gene

Two hundred and ninety-seven DBS specimens were extracted and amplified the reverse transcriptase (RT) and protease (PR) regions on *pol* gene by nested-PCR. The RT region was amplified using first set of primers (MJ3, MJ4, A(35) and NE1(35)) or alternative primer set (RT18, RT21, RT1 and RT4). The PR region was amplified using 5' prot 1, 3' prot 1, 5' prot 2 and 3' prot 2 primer. The final round amplified products were obtained from all samples. The size of PCR products were determined by 1% agarose gel electrophoresis. The size of RT region amplified product using first primer set was 798 bp, while RT region amplified product using alternative primer set was 647 bp, and PR region amplified product was 507bp.

The PCR products sizes were shown in Figure 3.1. There were 287 (96.6%) DBS samples that could be amplified at least 1 region. The 275 (95.8%) DBS samples were successfully amplified at the RT region, while 12 (4.2%) DBS samples were not amplified. In case of PR region amplification, there were 244 (85.0%) DBS samples were successfully amplified, while 44(15.0%) DBS samples were unable to be amplified.

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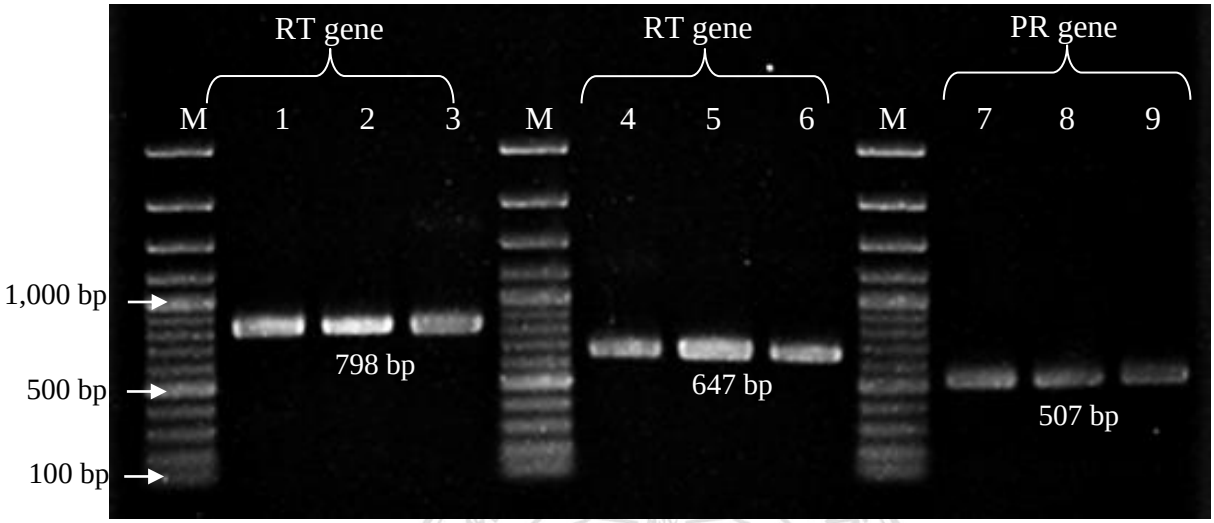

Figure 3.1 The PCR products sizes of reverse transcriptase and protease region on 1% agarose gel in 0.5X TAE

M = 100 bp ladder marker

Lane 1-3 = The 798 bp of RT region amplified products that using first set primers

Lane 4-6 = The 647 bp of RT region amplified products that using alternative set primers

Lane 7-9 = The 507 bp of PR region amplified products

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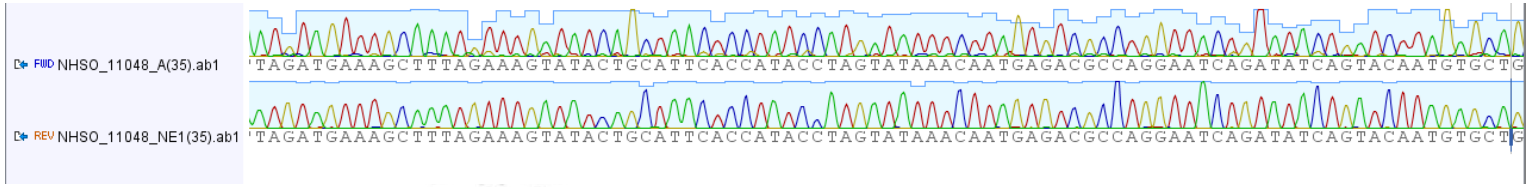
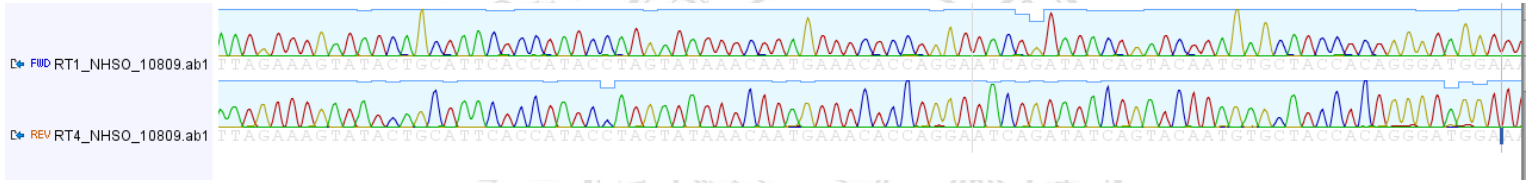
3.3 Sequence analysis

Two hundred and eighty seven nested-PCR products of RT and PR regions were analyzed by the dideoxy chain termination principle using the Big Dyeterminater V.3.1 cycle sequencing kit (Applied Biosystem, USA). The nucleotide was sequenced in both directions using the individual inner primer of RT and PR regions (A(35), NE1(35), RT1, RT4, 5’ prot 2 and 3’ prot 2) using the automatic ABI Prism 3100/3130 Genetic Analyzer (Applied Biosystems, USA). The figures of electropherogram of the RT and PR regions were shown in Figures 3.2.

(A) RT region nucleotide sequence using A(35) and NE1(35) primer.



(B) RT region nucleotide sequence using RT1 and RT4 primer.



(C) PR region nucleotide sequence using 5’ prot 2 and 3’ prot 2 primer.

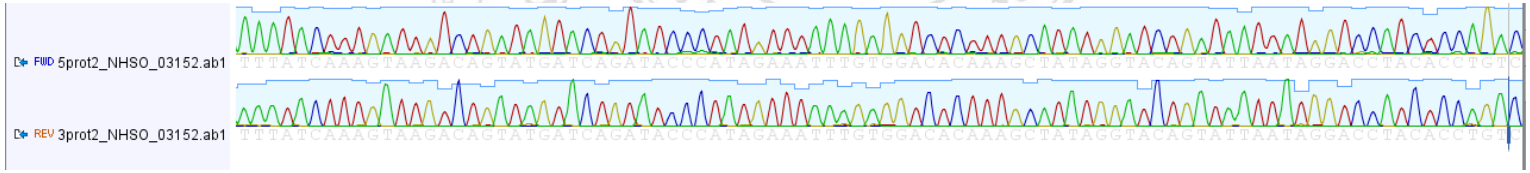


Figure 3.2 The electropherogram of nucleotide sequence in forward and reverse direction.

3.4 Interpretation of HIV drug resistance mutation (DRM) among newly HIV-1 infected infants.

The 275 RT region and 244 PR region nucleotide sequences were interpreted the HIV drug resistance mutation using the Stanford HIVdb Program Genotypic Resistance Interpretation Algorithm (Version 7. 0, last updated 02/ 27/ 14) . Any mutation or combination of mutation that produces potential-low, low, intermediate, or high level resistance to relevant NRTI, NNRTI or PI ARV drug is defined as drug resistant-HIV to that drug. The interpretation of drug resistance results were shown in Figure 3.3 and 3.4.

From interpretations, two hundred thirty of infants had no mutations associated with resistance to ARV drug. The mutations that associated with resistance to at least one family ARV drug were detected in 57 (19.9%) of all 287 infants. The DRMs by regions was 36 (13.1%) infants for RT region and 21 (8.6%) infants for PR regions. The summary of antiretroviral drug resistance mutations detected among newly HIV-1 infected infants was demonstrated in Table 3.2 and Figure 3.5. The resistance to NRTI, NNRTI and PI drugs was observed in 14 (5.1%), 25(9.1%), and 4 (1.6%) infants, respectively. Two (0. 7%) infants harbored ≥ 2 NRTI DRMs. Thymidine analog mutations (TAMs) were detected among 8 (2.9%) infants and ≥ 3 TAMs was not found. Five (1.8%) infants found ≥ 2 mutations which resistant to NNRTIs. More than 2 or 3 major PI DRMs in one patient was not observed. Three (1.1%) infants harbored both of NRTI and NNRTI mutations. The triple drug class resistance was not found in this study. The DRMs, predicted ARV resistance and ARV exposure data of individual HIV-1 infected infants were shown in Table 3.3.

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Table 3.2 Prevalence of drug resistant mutations (DRMs) to drug class family in HIV infected infants.

	n/N with DRMs (%)	**95% CI**
Infants with sequenced RT	36/275(13.1%)	
Infants with sequenced PR	21/244(8.6%)	
Prevalence of DRMs		
Resistance to any class (total)	57/287 (19.9%)	15.2-24.5
No DRMs	230/287 (80.1%)	
Resistance to NRTI	**14/275 (5.1%)**	**2.5-7.7**
≥2 NRTI DRMs	2/275 (0.7%)	
TAMs	8/275 (2.9%)	
≥ 3 TAMs	0/275 (0.0%)	
Resistance to NNRTIs	**25/275 (9.1%)**	**5.7-12.5**
≥ 2 NNRTI DRMs	5/275 (1.8%)	
Resistance to PIs (major)	**4/244 (1.6%)**	**0.3-3.2**
> 2-3 major PI DRMs	0/244 (0.0%)	
Resistance to two class (NRTI + NNRTI)	**3/275 (1.1%)**	
Resistance to three class (NRTI + NNRTI + PI major)	**0/287 (0.0%)**	

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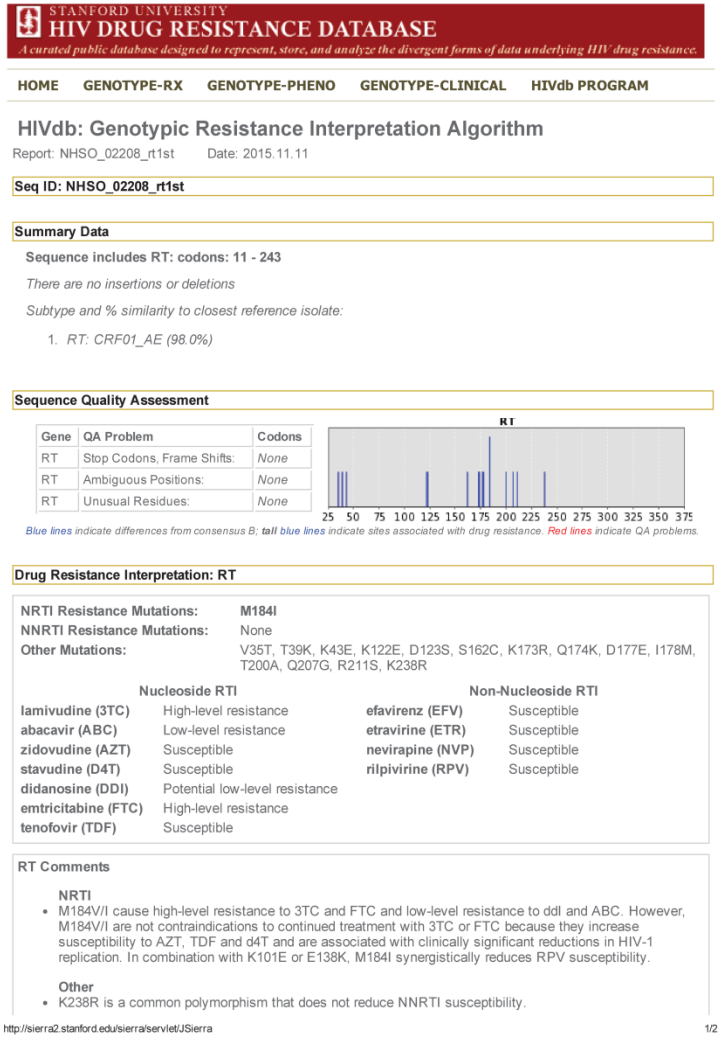

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HIV DRUG RESISTANCE DATABASE
A curated public database designed to represent, store, and analyze the divergent forms of data underlying HIV drug resistance.

HOME GENOTYPE-RX GENOTYPE-PHENO GENOTYPE-CLINICAL HIVdb PROGRAM

HIVdb: Genotypic Resistance Interpretation Algorithm

Report: NHSO_02208_rt1st Date: 2015.11.11

Seq ID: NHSO_02208_rt1st

Summary Data

Sequence includes RT: codons: 11 - 243

There are no insertions or deletions

Subtype and % similarity to closest reference isolate:

1. *RT: CRF01_AE (98.0%)*

Sequence Quality Assessment

Gene	QA Problem	Codons
RT	Stop Codons, Frame Shifts:	*None*
RT	Ambiguous Positions:	*None*
RT	Unusual Residues:	*None*

RT

25 50 75 100 125 150 175 200 225 250 275 300 325 350 375

Blue lines indicate differences from consensus B; tall blue lines indicate sites associated with drug resistance. Red lines indicate QA problems.

Drug Resistance Interpretation: RT

NRTI Resistance Mutations: **M184I**
NNRTI Resistance Mutations: None
Other Mutations: V35T, T39K, K43E, K122E, D123S, S162C, K173R, Q174K, D177E, I178M, T200A, Q207G, R211S, K238R

Nucleoside RTI		Non-Nucleoside RTI	
lamivudine (3TC)	High-level resistance	**efavirenz (EFV)**	Susceptible
abacavir (ABC)	Low-level resistance	**etravirine (ETR)**	Susceptible
zidovudine (AZT)	Susceptible	**nevirapine (NVP)**	Susceptible
stavudine (D4T)	Susceptible	**rilpivirine (RPV)**	Susceptible
didanosine (DDI)	Potential low-level resistance		
emtricitabine (FTC)	High-level resistance		
tenofovir (TDF)	Susceptible		

RT Comments

NRTI

- M184V/I cause high-level resistance to 3TC and FTC and low-level resistance to ddI and ABC. However, M184V/I are not contraindications to continued treatment with 3TC or FTC because they increase susceptibility to AZT, TDF and d4T and are associated with clinically significant reductions in HIV-1 replication. In combination with K101E or E138K, M184I synergistically reduces RPV susceptibility.

Other

- K238R is a common polymorphism that does not reduce NNRTI susceptibility.

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Mutation Scoring

RT	3TC	ABC	AZT	D4T	DDI	FTC	TDF	EFV	ETR	NVP	RPV
M184I	60	15	-10	-10	10	60	-10	-	-	-	-
Total:	60	15	-10	-10	10	60	-10	0	0	0	0

Database

- Citing Database
- Terms of Use / FAQs
- User Guide & Database Documents
- Database Statistics
- News

Resources

- HIV Treatment Websites
- RT, protease and integrase structures
- Additional Resources

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Figure 3.3 The interpretation DRM of RT region from the Stanford HIVdb Program Genotypic Resistance Interpretation Algorithm.

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A curated public database designed to represent, store, and analyze the divergent forms of data underlying HIV drug resistance.

HOME GENOTYPE-RX GENOTYPE-PHENO GENOTYPE-CLINICAL HIVdb PROGRAM

HIVdb: Genotypic Resistance Interpretation Algorithm

Report: NHSO_02208_pr1st Date: 2015.12.13

Seq ID: NHSO_02208_pr1st

Summary Data

Sequence includes PR: codons: 1 - 99

There are no insertions or deletions

Subtype and % similarity to closest reference isolate:

1. *PR: CRF01_AE (96.6%)*

Sequence Quality Assessment

Gene	QA Problem	Codons
PR	Stop Codons, Frame Shifts:	*None*
PR	Ambiguous Positions:	*None*
PR	Unusual Residues:	*None*

PR

0 10 20 30 40 50 60 70 80 90 100

Blue lines indicate differences from consensus B; tall blue lines indicate sites associated with drug resistance. Red lines indicate QA problems.

Drug Resistance Interpretation: PR

PI Major Resistance Mutations: None
PI Minor Resistance Mutations: **L33F**
Other Mutations: I13V, L19I, M36I, R41K, L63H, H69K, L89M, I93V

Protease Inhibitors

atazanavir/r (ATV/r)	Susceptible
darunavir/r (DRV/r)	Susceptible
fosamprenavir/r (FPV/r)	Potential low-level resistance
indinavir/r (IDV/r)	Susceptible
lopinavir/r (LPV/r)	Susceptible
nelfinavir (NFV)	Susceptible
saquinavir/r (SQV/r)	Susceptible
tipranavir/r (TPV/r)	Potential low-level resistance

PR Comments

PIMinor

- L33F is a relatively nonpolymorphic accessory mutation selected by DRV, FPV, LPV, NFV and TPV. In combination with other PI-resistance mutations, L33F is associated with reduced susceptibility to these PIs. It is included in the Tibotec DRV GSS.

Other

- L89M is a common polymorphism that is not associated with reduced PI susceptibility. It is the consensus amino acid in most non-B subtypes.

http://sierra2.stanford.edu/sierra/servlet/JSierra 1/2

Mutation Scoring

PR	ATV/r	DRV/r	FPV/r	IDV/r	LPV/r	NFV	SQV/r	TPV/r
L33F	5	5	10	0	5	5	0	10
Total:	5	5	10	0	5	5	0	10

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Figure 3.4 The interpretation DRM of PR region from the Stanford HIVdb Program Genotypic Resistance Interpretation Algorithm

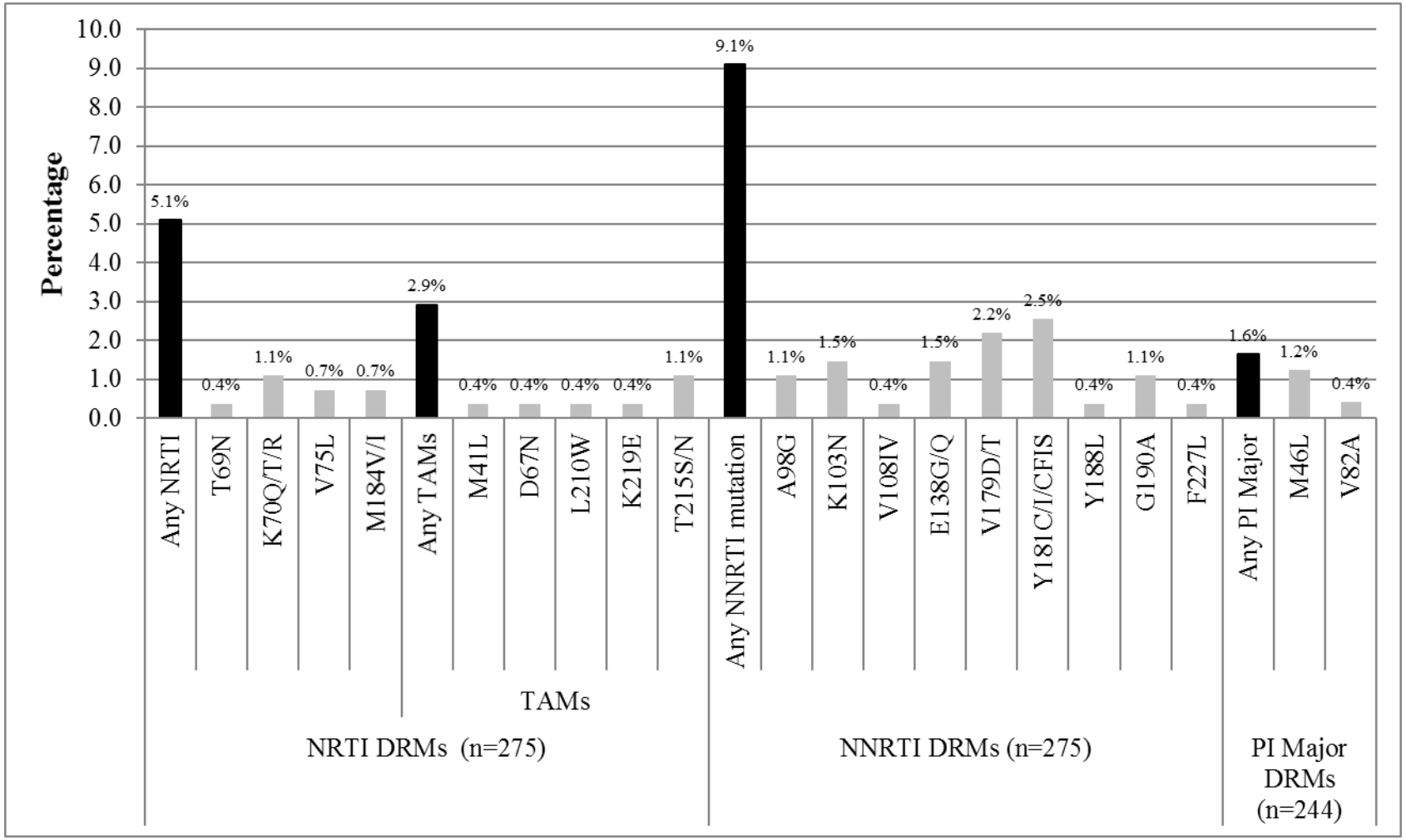

Figure 3.5 The summary of drug resistance mutations among newly HIV-1 infected infants.

Table 3.3 HIV-1 DRMs profiles, predicted ARV resistance and ARV exposure data among HIV-1 infected infants.

No.	Patient id	Age at sampling (months), [Birth Y/M]	RT DRM		PI DRMs		Affected drugs	Pre-labor maternal drugs (GA at ARV initiation, days)	Infant prophylaxis (Average time on ARVs, days)
			NRTI	NNRTI	Major	Minor			
1	CMU00179	NA [NA]	ND	ND	ND	K20I	NFV^{P}	NA	NA
2	CMU01222	2.1 [2007/11]	ND	ND	ND	L33F	FPV/r^{P},TPV/r^{P}	AZT (196.0)	AZT(7)
3	CMU01260	6.0 [2007/02]	ND	ND	ND	K20I	NFV^{P}	AZT (NA)	AZT(168)
4	CMU01789	9.9 [2008/10]	ND	ND	ND	K20I	NFV^{P}	none	none
5	CMU02026	9.7 [2007/07]	ND	F227L	ND	ND	NVP^{I},EFV^{L}	NA	AZT(7),sdNVP
6	CMU02208	2.1 [2007/11]	**M184I**	ND	ND	L33F	**$3TC^{H}$,FTC^{H}**,ABC^{L},DDI^{P}, FPV/r^{P}, TPV/r^{P}	AZT(NA), sdNVP	AZT(NA), sdNVP
7	CMU02209	1.9 [2007/11]	ND	**G190A**	ND	ND	**NVP^{H}**, EFV^{I},ETR^{L},RPV^{L}	none	AZT(2hr.), sdNVP
8	CMU02335	2.7 [2008/05]	ND	V179D	ND	ND	EFV^{P},ETR^{P},NVP^{P},RPV^{P}	AZT (196.0), sdNVP	AZT(7), sdNVP

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Table 3.3 (Continued)

No.	Patient id	Age at sampling (months), [Birth Y/M]	RT DRM		PI DRMs		Affected drugs	Pre-labor maternal drugs (GA at ARV initiation, days)	Infant prophylaxis (Average time on ARVs, days)
			NRTI	NNRTI	Major	Minor			
9	CMU02456	8.7 [2008/09]	ND	ND	ND	K20I	NFV^{L}	none	none
10	CMU02472	2.7 [2011/09]	ND	ND	ND	T74S	NFV^{L}	NA	AZT(7)
11	CMU03036	4.7 [2008/06]	ND	ND	**M46L**	ND	NFV^{L},ATV/r^{P},FPV/r^{P},IDV/r^{P}, LPV/r^{P},TPV/r^{P}	AZT(126)	AZT(42), sdNVP
12	CMU03194	4.1 [2008/10]	ND	ND	ND	K20I	NFV^{P}	AZT(196)	AZT(13)
13	CMU03284	3.4 [2008/10]	ND	A98G, **Y181C**	ND	ND	**NVP^{H}**,RPV^{I},ETR^{I},EFV^{I}	AZT(273), sdNVP	AZT(42), sdNVP
14	CMU03302	5.2 [2010/01]	K70Q, V75L	**Y181C**	ND	ND	$D4T^{L}$,DDI^{L},$3TC^{P}$,ABC^{P},FTC^{P}, TDF^{P},**NVP^{H}**,EFV^{I},ETR^{I},RPV^{I}	AZT(NA), sdNVP	AZT(42), sdNVP
15	CMU03461	5.9 [2008/03]	T215S	ND	ND	ND	AZT^{L},$D4T^{L}$,ABC^{P},DDI^{P}	AZT(196)	AZT(42)
16	CMU03785	0.4 [2009/04]	ND	E138G	NA	NA	RPV^{L},EFV^{P},ETR^{P},NVP^{P}	AZT(NA)	AZT(1)

Table 3.3 (Continued)

No.	Patient id	Age at sampling (months), [Birth Y/M]	RT DRM		PI DRMs		Affected drugs	Pre-labor maternal drugs (GA at ARV initiation, days)	Infant prophylaxis (Average time on ARVs, days)
			NRTI	NNRTI	Major	Minor			
17	CMU03887	3.8 [2009/03]	ND	**Y181C**	ND	ND	**NVP^{H}**,EFV^{I},ETR^{I},RPV^{I}	AZT(196)	AZT(7), sdNVP
18	CMU04036	1.9 [2008/11]	ND	ND	ND	L33F	FPV/r^{P},TPV/r^{P}	AZT(196)	AZT(6hr)
19	CMU04216	3.4 [2009/10]	ND	**G190A**	ND	ND	**NVP^{H}**, EFV^{I},ETR^{L},RPV^{L}	none	AZT(42), sdNVP
20	CMU04774	3.1 [2009/10]	ND	**Y181C**	ND	ND	**NVP^{H}**,EFV^{I},ETR^{I},RPV^{I}	AZT(196)	AZT(NA), sdNVP
21	CMU05065	5.2 [2010/03]	ND	ND	ND	L33F	FPV/r^{P},TPV/r^{P}	none	AZT(NA)
22	CMU05252	3.2 [2010/10]	ND	E138G	ND	ND	RPV^{L},EFV^{P},ETR^{P},NVP^{P}	AZT(NA)	AZT(NA), sdNVP
23	CMU05282	3.4 [2010/03]	ND	V179D	ND	ND	EFV^{P},ETR^{P},NVP^{P},RPV^{P}	AZT(252)	none
24	CMU05305	5.6 [2010/07]	ND	A98G**,** **Y181C**	ND	ND	**NVP^{H}**,EFV^{I},ETR^{I},RPV^{I}	HAART*	NA

Table 3.3 (Continued)

No.	Patient id	Age at sampling (months), [Birth Y/M]	RT DRM		PI DRMs		Affected drugs	Pre-labor maternal drugs (GA at ARV initiation, days)	Infant prophylaxis (Average time on ARVs, days)
			NRTI	NNRTI	Major	Minor			
25	CMU05342	2.5 [2010/01]	ND	A98G, V179T	ND	ND	EFV^{L},ETR^{L},RPV^{L},NVP^{I}	AZT(196), sdNVP	AZT(42)
26	CMU05427	4.2 [2010/06]	ND	ND	ND	K20I	NFV^{P}	none	AZT(NA)
27	CMU05601	8.3 [2009/08]	V75L	ND	ND	ND	$D4T^{P}$,DDI^{P}	AZT(NA)	AZT(42), sdNVP
28	CMU05787	2.6 [2010/03]	ND	**Y181I**	ND	ND	**NVP^{H},ETR^{H},RPV^{H}**,EFV^{I}	ARVs*	AZT(NA), sdNVP
29	CMU05969	4.4 [2010/02]	**L210W**	ND	ND	K20I	AZT^{L},$D4T^{L}$,ABC^{P},DDI^{P}, TDF^{P},NFV^{P}	AZT(NA), sdNVP	sdNVP
30	CMU07620	1.0 [2011/01]	K70T	ND	ND	ND	$3TC^{P}$,ABC^{P},$D4T^{P}$,DDI^{P}, FTC^{P},TDF^{P}	NA	AZT(NA)
31	CMU07733	3.9 [2010/09]	ND	ND	ND	L23I	NFV^{L}	AZT(NA), sdNVP	AZT(NA), sdNVP
32	CMU07904	1.4 [2012/03]	ND	ND	ND	K20I	NFV^{P}	AZT(NA), sdNVP	AZT(42),NVP (28),3TC(42)

Table 3.3 (Continued)

No.	Patient id	Age at sampling (months), [Birth Y/M]	RT DRM		PI DRMs		Affected drugs	Pre-labor maternal drugs (GA at ARV initiation, days)	Infant prophylaxis (Average time on ARVs, days)
			NRTI	NNRTI	Major	Minor			
33	CMU08524	2.8 [2010/11]	**M41L**	ND	ND	ND	AZT^{L},D4T^{L},ABC^{P},DDI^{P},TDF^{P}	AZT(NA), sdNVP	AZT(NA), sdNVP
34	CMU08526	3.6 [2011/04]	ND	ND	ND	L33F	FPV/r^{P},TPV/r^{P}	AZT,3TC,LPV/r (238)	AZT(28)
35	CMU08585	1.3 [2011/04]	**K219E**	**K103N**	ND	ND	AZT^{P},DDI^{P},**NVP^{H},EFV^{H}**	none	none
36	CMU08684	2.0 [2011/05]	ND	ND	**M46L**	ND	NFV^{L},ATV/r^{P},FPV/r^{P},IDV/r^{P}, LPV/r^{P},TPV/r^{P}	AZT,3TC,LPV/r (266)	AZT(17hr)
37	CMU08696	2.0 [2012/05]	**M184V**	**K103N**	ND	ND	**3TC^{H},FTC^{H}**,ABC^{L},DDI^{P},**EFV^{H}, NVP^{H}**	AZT,3TC,LPV/r (154)	AZT(28)
38	CMU08791	2.5 [2011/06]	ND	**Y188L**	ND	ND	**NVP^{H},EFV^{H},RPV^{H}**,ETR^{L}	NVP,3TC,d4T (35)	AZT(28)
39	CMU09040	2.2 [2011/12]	ND	**Y181CFIS**	ND	ND	**NVP^{H},ETR^{H},RPV^{H}**,EFV^{I}	AZT, 3TC, NVP (0)	AZT(28), sdNVP
40	CMU09420	1.1 [2011/10]	ND	V179T	ND	ND	EFV^{P},ETR^{P},NVP^{P},RPV^{P}	none	AZT(42),NVP (28), 3TC(42)

Table 3.3 (Continued)

No.	Patient id	Age at sampling (months), [Birth Y/M]	RT DRM		PI DRMs		Affected drugs	Pre-labor maternal drugs (GA at ARV initiation, days)	Infant prophylaxis (Average time on ARVs, days)
			NRTI	NNRTI	Major	Minor			
41	CMU10259	2.5 [2012/03]	T215S	ND	ND	ND	AZT^{L},$D4T^{L}$,ABC^{P},DDI^{P}	none	none
42	CMU10724	1.6 [2012/04]	ND	**V108IV**	NA	NA	NVP^{L},EFV^{P}	HAART*	none
43	CMU10982	1.1 [2012/07]	ND	E138Q	NA	NA	RPV^{L},EFV^{P},ETR^{P},NVP^{P}	AZT,TDF,LPV/r (NA)	AZT(NA), sdNVP
44	CMU11334	1.0 [2012/07]	ND	ND	ND	K20I	NFV^{L}	AZT,3TC,LPV/r (98)	AZT(28)
45	CMU11462	8.0 [2012/05]	**D67N, K70R**	ND	ND	ND	AZT^{I},$D4T^{I}$,ABC^{L},DDI^{L},TDF^{L},	AZT,NVP,3TC (NA)	AZT(28)
46	CMU12500	3.7 [2012/11]	**M41L**	ND	ND	ND	AZT^{L},$D4T^{L}$,ABC^{P},DDI^{P},TDF^{P}	AZT,3TC,LPV/r (140)	AZT(28)
47	CMU12739	8.6 [2012/08]	ND	**K103N**, E138G	NA	NA	**EFV^{H},NVP^{H}**,RPV^{L},ETR^{P}	none	none
48	CMU13051	7.2 [2012/11]	ND	ND	ND	K20I	NFV^{L}	none	none

Table 3.3 (Continued)

No.	Patient id	Age at sampling (months), [Birth Y/M]	RT DRM		PI DRMs		Affected drugs	Pre-labor maternal drugs (GA at ARV initiation, days)	Infant prophylaxis (Average time on ARVs, days)
			NRTI	NNRTI	Major	Minor			
49	CMU13124	2.0 [2013/05]	ND	ND	ND	L33F	FPV/r^{P},TPV/r^{P}	none	AZT(42),NVP (28),3TC(42)
50	CMU13181	11.5 [2012/09]	ND	**G190A**	ND	ND	**NVP^{H}**,ETR^{L},RPV^{L},EFV^{I}	none	none
51	CMU13823	5.9 [2014/05]	ND	ND	**M46L**	ND	NFV^{L},ATV/r^{P},FPV/r^{P},IDV/r^{P}, LPV/r^{P},TPV/r^{P}	AZT,3TC,LPV/r (154)	AZT(28)
52	CMU13917	1.7 [2014/06]	ND	ND	ND	K20I	NFV^{P}	none	AZT(42)
53	CMU14812	1.0 [2014/08]	ND	V179D	ND	ND	EFV^{P},ETR^{P},NVP^{P},RPV^{P}	AZT,3TC,LPV/r (112)	AZT(42),NVP (28),3TC(42)
54	CMU15047	2.0 [2014/03]	T69N	ND	NA	NA	DDI^{P}	none	AZT(28),NVP (14),3TC(28)
55	CMU15202	2.9 [2014/07]	ND	**K103N**, V179T	NA	NA	**EFV^{H},NVP^{H}**,ETR^{P},RPV^{P}	AZT(252), sdNVP	AZT,NVP,3TC (NA)
56	CMU15208	3.9 [2014/05]	ND	ND	**V82A**	ND	ATV/r^{L},FPV/r^{L},SQV/r^{L},IDV/r^{I}, LPV/r^{I},NFV^{I}	none	none

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Table 3.3 (Continued)

No.	Patient id	Age at sampling (months), [Birth Y/M]	RT DRM		PI DRMs		Affected drugs	Pre-labor maternal drugs (GA at ARV initiation, days)	Infant prophylaxis (Average time on ARVs, days)
			NRTI	NNRTI	Major	Minor			
57	CMU15756	5.4 [2014/10]	T215N	ND	NA	NA	AZT^{L},D4T^{L},ABC^{P},DDI^{P}	none	none

ND, not detected DRMs; NA; No available data; *, No available drug data.

GA, gestational age, sdNVP, single dose nevirapine (received at delivery in mother and at postpartum in infants).

Bold type, Major mutations according to the Stanford HIV database were in bold.

RT DRM, reverse transcriptase drug resistance mutation, NRTI, nucleoside/nucleotide reverse transcriptase inhibitors; NNRTI, non-nucleoside reverse transcriptase inhibitors

PI DRMs, protease inhibitor drug resistance mutations; Major, PI Major resistance mutations; Minor, PI Minor resistance mutations.

EFV, efavirenz; ETR, etravirine, NVP, nevirapine; RPV, rilpivirine; 3TC, lamivudine; ABC, abacavir; AZT, zidovudine; D4T, stavudine; DDI, didanosine; FTC, emtricitabine; TDF, tenofovir.

ATV/r, atazanavir/r; DRV/r, darunavir/r; FPV/r, fosamprenavir/r; IDV/r, indinavir/r; LPV/r, lopinavir/r; NFV, nelfinavir; SQV/r, saquinavir/r; TPV/r, tipranavir/r.

^{P}, potential-low level resistance; ^{L}, low level resistance; ^{I}, intermediate level resistance; and **bold type**^{H}, high level resistance to ARV drug.

3.4.1 HIV DRMs profiles on reverse transcriptase region.

Among 275 HIV-1 infected infants that the RT region sequence data was available. The HIV-1 drug resistance mutations (DRMs) were found in 36 (13.1%) infants. The summary of reverse transcriptase inhibitors mutations was shown in Table 3.4.

The NRTI mutations were determined in 14 infants. The prevalence of NRTI mutation was 5.1%, 95% CI (2.4-7.7). The major mutations of NRTI, M184V/I and K70Q/R/T were found in 2 (0.7%) and 3(1.1%) infants, respectively. The T69N and V75L mutations were also observed. T69N was found in 1 (0.4%) infants and V75L was found in 2 (0.7%) infants.

TAMs were detected among 8 (2.9%) infants and reported as M41L, D67N, L210W, K219E were found in 1 (0.4%) infants, and T215S/N were found in 3 (1.1%). Greater than 2 TAMs were not detected.

The NNRTI mutations were observed in 25 infants. The NNRTI mutations prevalence was 9.1%, 95% CI (5.7-12.5). The most common NNRTI mutation was Y181C/I/CFIS. This mutation was demonstrated in 7 (2.5%) infants, followed by V179D/T that was found in 6 (2.2%) infants. K103N mutation was found in 4 (1.5%) infants. The E138G/Q was shown in 4 (1.5%) infants. The G190A was observed in 3 (1.1%) infants, A98G in 3 (1.1%) infants, Y188L in 1 (0.4%) infant, F227L in 1 (0.4%) infant and V108IV in 1 (0.4%) infant. Furthermore, the polymorphism mutations that responsible for the minimal effect to NNRTIs susceptibility such as V90I and V106I were observed. V90I was found in 2 (0.7%) infants and V106I was demonstrated in 3 (1.1%) infants.

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Three (2.9%) infants had virus with mutations that confer resistance to NRTI and NNRTI drugs. One infant carried the K70Q, V75L, and Y181C mutations. The second infant harbored the K219E and K103N mutations. The last infant had M184V and K103N mutations. Two of three infants had been exposed to PMTCT.

In 227 (82.5%) of 275 infants had been exposed to PMTCT. Among 227 PMTCT-exposed infants, 31 (13.7%) infants had DRMs on RT region. These DRMs included

NRTI mutations in 11(4.9%) infants and NNRTI mutations in 22 (9.7%) infants. The most common NNRTI DRMs was Y181C/I/FS constituting 7 (22.6%) of 31 infants and this mutation cause resistance to NVP. Moreover, 111 (48.9%) of 227 PMTCT-exposed infants had exposed sdNVP. In sdNVP-exposed infants, the NNRTI mutations were found in 14 (12.6%) infants. The most patterns of DRMs in sdNVP-exposed infants was Y181C/I/CIFS in 6 infants. The G190A mutation was found in 2 infants.

Among 44 PMTCT-unexposed infants, 5 (11.4%) infants had DRMs. This included NRTI DRMs 3 (6.8%) infants and NNRTI DRMs 3 (6.8%) infants. The most common NNRTI mutation was K103N in 2 infants and this mutation confer resistant to EFV and NVP.

The remaining 4 (1.5%) infants had no available PMTCT-exposed data, nevertheless, the mutation was not found.

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Table 3.4 Reverse transcriptase inhibitors resistant mutations in HIV infected infants.

Mutation Point	Number (%), (n=275)
Any RT mutation	36 (13.1%)
NRTI mutations	11 (4.0%)
NNRTI mutations	22 (8.0%)
NRTI+ NNRTI mutations	3 (1.1%)
NRTI mutations	
T69N	1 (0.4%)
K70Q/T/R	3 (1.1%)
V75L	2 (0.7%)
M184V/I	2 (0.7%)
TAMs	
M41L	1 (0.4%)
D67N	1 (0.4%)
L210W	1 (0.4%)
K219E	1 (0.4%)
T215S/N	3 (1.1%)
Any NRTI mutation	14 (5.1%)
1 NRTI mutation	12 (4.4%)
2 NRTI mutation	2 (0.7%)
Any TAMs	8 (2.9%)
≥ 3 TAMs	0 (0.0%)
NNRTI mutations	
A98G	3 (1.1%)
K103N	4 (1.5%)
V108IV	1 (0.4%)
E138G/Q	4 (1.5%)
V179D/T	6 (2.2%)
Y181C/I/CFIS	7 (2.5%)
Y188L	1 (0.4%)
G190A	3 (1.1%)
F227L	1 (0.4%)
Any NNRTI mutation	25 (9.1%)
1 NNRTI mutation (per patient)	20 (7.2%)
2 NNRTI mutation (per patient)	5 (1.8%)

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3.4.2 HIV DRM profiles on protease region

The protease region nucleotide sequencing data were available in 244 HIV-1 infected infants. The PI DRMs were shown in 24 (9.8%) infants. Of the 24 infants, 4 (1.6%) infants demonstrated the PI major mutations, whereas 20 (8.2%) infants shown the PI minor mutations. The prevalence of major PI DRMs were found in 1.6%, 95% CI (0.3-3.2).

The major PI mutations including M46L and V82A were found. Three (1.2%) infants harbored M46L and 1 (0.4%) infants harbored V82A. The major M46L is nonpolymorphic PI-selected mutations that reduce susceptibility to IDV, NFV, FPV, LPV and ATV when present with other mutations. And V82A mutation is a nonpolymorphic substrate-cleft mutation that reduces susceptibility to IDV and causes cross-resistance to ATV and NFV. Interestingly, LPV and ATV, which is the third PI drug, recommended for use in HAART regimen for both children and adults. Greater than 2 major PI mutations were not detected.

The minor PI mutations such as K20I, L23I, L33F and T74S were found in 10 (4.1%), 1 (0.4%), 7 (2.9%) and 2 (0.8%) infants (Table 3.5).

L10V/I are polymorphic mutations that were observed in 38 infants (15.6%) on protease region determination. It is PI-selected accessory mutations that reduce PI susceptibility or increase the replication of viruses if accumulate with other PI-resistance mutations. Hence, it usually has little effect on PI susceptibility when occur without other DRMs.

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In 203 (83.2%) of 244 infants had been exposed to PMTCT. Among 203 PMTCT- exposed infants, 19 (9.4%) infants had DRMs on PR region. These DRMs included major PI mutations in 3(1.5%) infants and minor PI mutations in 16 (7.9%) infants. The most common major PI DRMs was M46L in 3 infants. In 2 of 3 infants who carried M46L had been exposed to maternal HAART that included LPV/r.

Among 37 PMTCT-unexposed infants, 4 (10.8%) infants had DRMs. This included major PI DRMs 1 (2.7 %) infants and minor PI DRMs 3 (8.1%) infants. The pattern of major PI mutation was V82A.

The remaining 4 (1.6%) infants had no available PMTCT-exposed data; however, the major PI DRMs were not observed in this group.

Table 3.5 Protease inhibitors resistant mutations in infected infants.

Mutation Point	Number (%) (n=244)
PI mutations	
Any PR mutation	24 (9.8%)
Major mutation	4 (1.6%)
M46L	3 (1.2%)
V82A	1 (0.4%)
Minor mutation	
K20I	10 (4.1%)
L23I	1 (0.4%)
L33F	7 (2.9%)
T74S	2 (0.8%)

3.4.3 Drug susceptibility interpretation

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Prediction of drug susceptibility to ARV drugs was interpreted using the HIV-1 RT region sequences obtained from 275 infants that carried out genotypic resistance interpretation for each reverse transcriptase inhibitor drugs. For each protease inhibitors, the interpretation used the HIV-1 PR region sequences from 244 infants. The predicted susceptibility to each of drugs was summarized in Figure 3.6.

In case of NRTI drugs, the results demonstrated that around 95% of patients were susceptible to NRTI family and around 5% of patients had resistance. The highest resistance rate for NRTI family was found mainly to FTC and 3TC with nearly 2% of patients having resistance, followed by AZT and D4T with, DDI, ABC, and TDF.

For NNRTIs, the results demonstrated that around 90% of patients were susceptible and around 10% of patients had resistance to NNRTI drug. The NVP account the highest levels of resistance, followed by EFV, RPV, and ETR.

Predicting of PIs susceptibility, the results demonstrated that around 96% of patients were susceptible to PI and around 4% of patients had resistance. The highest predicted level of resistance was for NFV, followed by LPV/r, IDV/r, FPV/r, ATV/r, SQV/r, and TPV/r. For DRV/r, genotypic resistance interpretation indicated an absence of any level of resistance.

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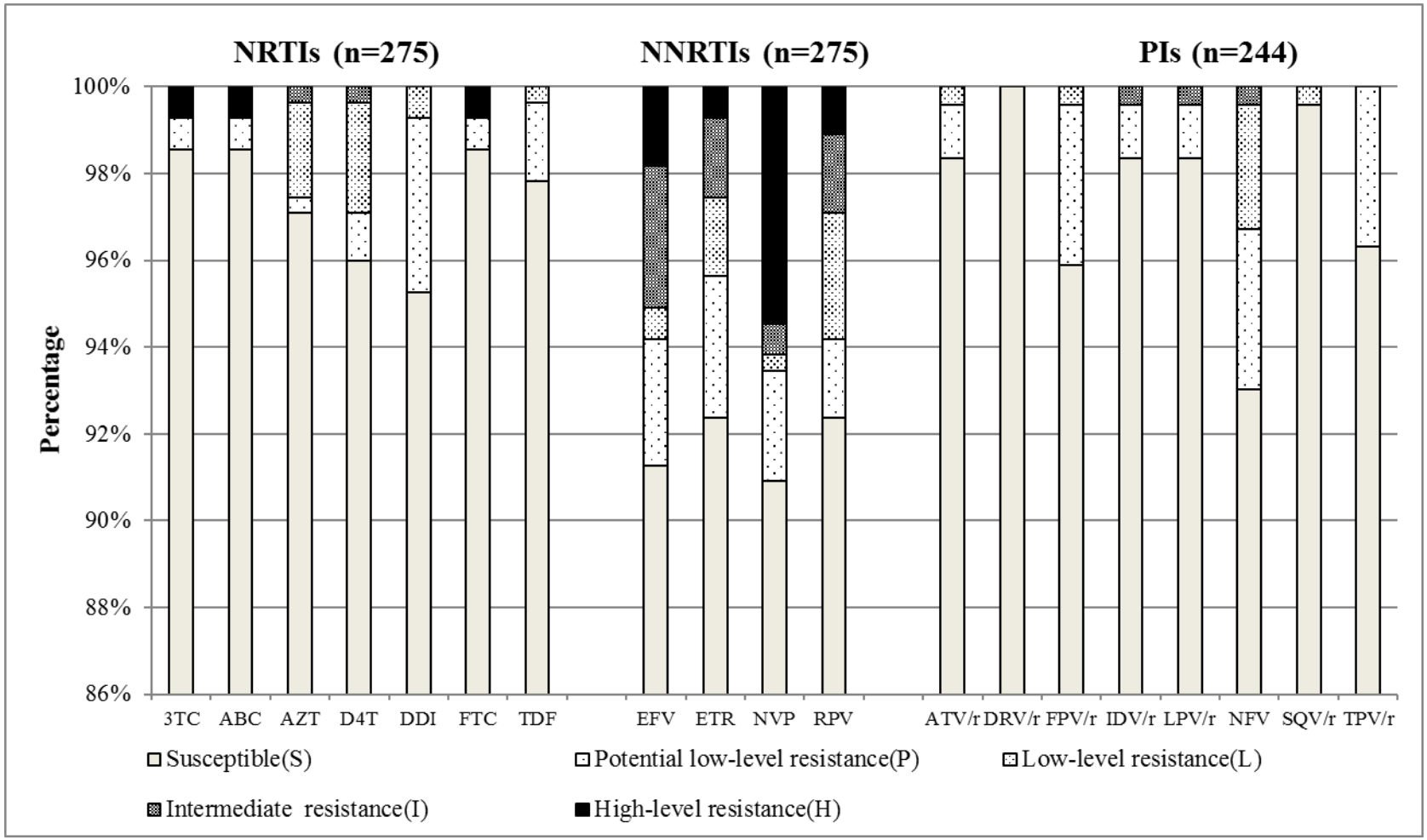

Figure 3.6 Predicted susceptibility to each ARV drug class, including NRTIs, NNRTIs and PIs.

3.5 Genetic subtype of HIV-1 among patients

3.5.1 The Stanford HIVdb Program Genotypic Resistance Interpretation Algorithm

From drug resistance mutations interpretation of RT region in 275 infants, the HIV-1 subtype were identified as CRF01_AE in 255 infants (92.7%), subtype B in 19 infants (6.9%), and subtype C in 1 infant (0.4%).

Moreover, the interpretation of HIV-1 subtype of PR region in 244 samples were found as CRF01_AE in221 infants (91.4%), subtype B in 22 infants (8.2%) and subtype C in 1 infant (0.4%).

Of the 287 infants, 265 (92.3%) of infants were infected with HIV-1 subtype CRF01_AE, HIV-1 subtype B were found in 21 (7.3%) of infants and HIV-1 subtype C was found in 1 (0.4%) of infant. The HIV-1 subtype results were shown in Table 3.6.

Table 3.6 HIV-1 subtype by The Stanford HIVdb Program Genotypic Resistance Interpretation Algorithm

Subtype	RT region (%) (n=275)	PR region (%) (n=244)	All (%) (n=287)
CRF01_AE	255 (92.7)	223 (91.4)	265 (92.3)
B	19 (6.9)	20 (8.2)	21 (7.3)
C	1 (0.4)	1 (0.4)	1 (0.4)

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3.5.2 REGA HIV-1 Subtyping analysis

The HIV-1 variants from DRMs interpretation were compared with HIV-1 genotypic results from REGA HIV-1 Subtyping analysis. The results showed the concordance between two tools.

Of the 287 infants, 255 (92.7%) of infants were infected with HIV-1 subtype CRF01_AE, HIV-1 subtype B were found in 19 (6.9%) of infants, and HIV-1 subtype C were found in 1 (0.4%) of infants. The HIV-1 subtype results were shown in Table 3.7.

Table 3.7 HIV-1 subtype results by REGA HIV-1 Subtyping Tool.

Subtype	**RT region (%) (n=275)**	**PR region (%) (n=244)**	**All (%) (n=287)**
CRF01_AE	255 (92.7)	223 (91.4)	265 (92.3)
B	19 (6.9)	20 (8.2)	21 (7.3)
C	1 (0.4)	1 (0.4)	1 (0.4)

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3.6 The infants and maternal factor analysis

The HIV drug resistance mutations results were further analyzed using data from HIV-1 infected infant and their mother status to analyze the association between the DRMs status and their characteristic by chi-square test.

The age of infants was considered for analyzing the relative with DRMs occurrence. The results showed that the age of infants had no significant difference in the occurrence of detectable DRMs.

The DRMs results and gender of infants demonstrated that female infants harbored NRTI, NNRTI and PI major DRM as 7 (5.6%), 14 (9.3%) and 1 (0.8%) infants, respectively. In case of male infants, 7 (4.7%), 11 (8.8%), and 3 (2.6%) infants demonstrated NRTI, NNRTI and PI DRM, respectively. These results showed that the gender of infants had no significant difference in the occurrence of NRTI, NNRTI and PI drug resistance mutations (p=0.726, 0.878 and 0.268, respectively).

The signs of HIV infection may affect the emergence of DRMs in infants. The NRTI, NNRTI and major PI DRMs were reported in 10 (5.0%), 19 (9.6%), and 2 (1.1%) infants without signs of HIV infection. In contrast, infants with signs of HIV infection harbored NRTI, NNRTI and major PI DRMs in 3 (5.8%), 6 (11.5%), and 2 (4.4%) infants. The results demonstrated that the infants with signs of HIV infection had no significant difference in the occurrence of NRTI, NNRTI DRMs and PI major DRMs (p= 0.829, 0.670 and 0.136), with 24 (NRTI/NNRTI) and 22 (major PI) missing data.

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The using ARV drugs for PMTCT are the main factor that associated to the occurrence DRMs in infected infants. In Thailand, there were 3 main national guidelines of PMTCT including 2006/2007, 2010, and 2014. The evidence of DRMs according to the year and month of birth was summarized into different drug families (Figure 3.7). The DRMs were detected in 2006/01-2010/08 that conferred the resistance to PIs (0.7%), NNRTIs (9.2%), and NRTIs (3.5%). During 2010/09-2014/08, the evidence of DRMs was mostly found in that period. These DRMs were responsible for PIs (2.2%), NNRTIs (9.0%), and NRTIs (6.2%) resistance. Since 2014/09, the DRMs with resistance to NRTIs were found in 9.1% of infants. One infected infant who had no available birth year and month data infected with wild type HIV. The statistical results

showed that the infants and PMTCT process following Thailand's guideline in each year had no significant difference in the occurrence of NRTI, NNRTI DRMs and PI major DRMs (p= 0.493, 0.615 and 0.476), with 1 missing data.

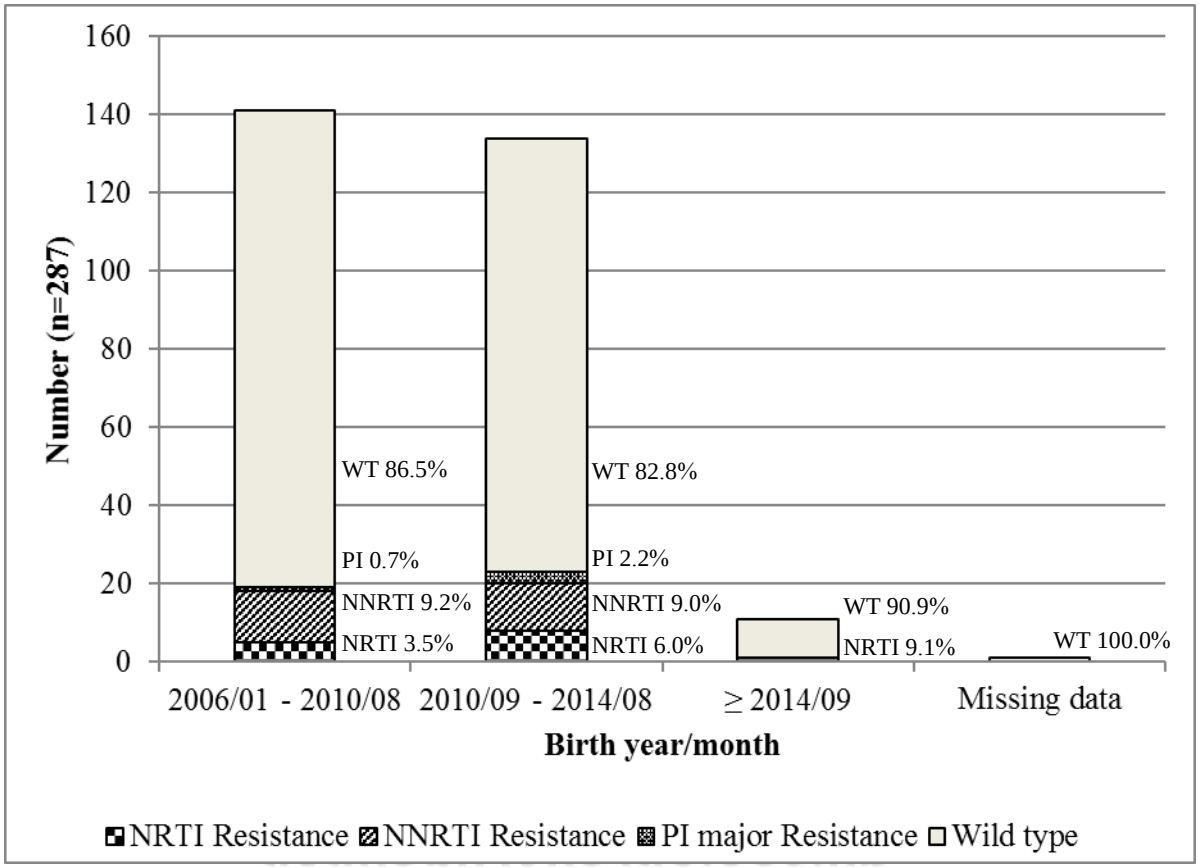

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Figure 3.7 HIV drug resistance mutations (DRMs) in infected infants by year/month of birth.

Infant prophylaxis using ARV drugs for PMTCT is the main factor that associated to the occurrence DRMs. In case of infants without prophylaxis receiving, the number of infants with DRMs had no significant difference when compare to prophylaxis receiving group with p-value = 0.724, 0.696 and 0.625 of NRTI, NNRTI and PI major DRM, respectively.

In case of infants who only received AZT prophylaxis, NRTI, NNRTI and PI DRMs that were observed in 5(6.0%), 4(4.8%) and 2(2.7%) infants. In sdNVP prophylaxis receiving group, NRTI DRM was found in 1 (33.3%) infant. Infants who received both AZT/sdNVP prophylaxis found NRTI, NNRTI, and major PI DRMs in 4(4.1%), 12(12.2%) and 1 (1.1%) infants, respectively. In AZT/NVP/3TC prophylaxis receiving group, NRTI and NNRTI DRMs were found in 1 (3.7%) and 3 (11.1%) infants. The results showed that the infants prophylaxis with ARV drugs had no significant difference in the occurrence of NRTI, NNRTI and PI major DRMs (p= 0.458, 0.464 and 0.872).

In case of the infants who were born to HIV infected mothers who received prophylaxis for PMTCT, the DRMs were found and had no significant difference when compared with non-prophylaxis receiving group (p-value = 0.562, 0.157, and 0.568)

The comparison of the infants who were born to HIV infected mothers who received MTCT prophylaxis only AZT, AZT/sdNVP and HAART had no significant difference in the occurrence of NRTI, NNRTI and major PI DRMs (p= 0.554, 0.586 and 0.482).

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Moreover, HIV-1 variants of patients had no significant difference in the demonstration of NRTI, NNRTI and PI major DRMs (p-value = 0.973, 0.791 and 0.826).

The association of characteristics and demographic parameters and HIV-1 DRMs in HIV-1 infected infants was shown in Table 3.8.

Table 3.8 The association of characteristics and demographic parameters and HIV-1 NRTI, NNRTI and PI major DRMs among HIV-1 infected infants.

	n/N (%) with NRTI DRMs (N=275)	***P* value**	**n/N (%) with NNRTI DRMs (N=275)**	***P* value**	**n/N (%) with PI DRMs (N=244)**	***P* value**
Age at sampling (months)						
≤1.0	1/6(16.7)		2/6(33.3)		0/5(0.0)	
1.1-2.0	3/80(3.8)		8/80(10.0)		1/66(1.5)	
2.1-3.0	4/93(4.3)		9/93(9.7)		0/86(0.0)	
3.1-4.0	1/25(4.0)		1/25(4.0)		1/22(4.6)	
4.1-5.0	1/22(4.6)		1/22(4.6)		1/21(4.8)	
≥5.0	4/48(8.3)	0.671	4/48(8.3)	0.333	1/43(2.3)	0.542
Missing data	0/1(0.0)		0/1(0.0)		0/1(0.0)	
Birth year/month						
2006/01– 2010/08	5/133(3.8)		13/133(9.8)		1/124(0.8)	
2010/09 – 2010/08	8/132(6.1)		12/132(9.1)		3/110(2.7)	
≥ 2014/09	1/9(11.1)	0.493	0/9(0.0)	0.615	0/9(0.0)	0.476
Missing data	0/1(0.0)		0/1(0.0)		0/1(0.0)	
Gender						
Female	7/150(5.6)		14/150(9.3)		1/128(0.8)	

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Table 3.8 (Continued)

	n/N (%) with NRTI DRMs (N=275)	*P* value	n/N (%) with NNRTI DRMs (N=275)	*P* value	n/N (%) with PI DRMs (N=244)	*P* value
Male	7/125(4.7)	0.726	11/125(8.8)	0.878	3/116(2.6)	0.268
Sign of infection						
No	10/199(5.0)		19/199(9.6)		2/177(1.1)	
Yes	3/52(5.8)	0.829	6/52(11.5)	0.670	2/45(4.4)	0.136
Missing data	1/24(4.2)		0/24(0.0)		0/22(0.0)	
Infant prophylaxis						
No	3/48(6.3)		5/48(10.4)		1/38(2.6)	
Yes	11/220(5.0)	0.724	19/220(8.6)	0.696	3/198(1.5)	0.625
Missing data	0/7(0.0)		1/7(14.2)		0/8(0.0)	
AZT	5/83(6.0)		4/83(4.8)		2/74(2.7)	
sdNVP	1/3(33.3)		0/3(0.0)		0/3(0.0)	
AZT/sdNVP	4/98(4.1)		12/98(12.2)		1/90(1.1)	
AZT/NVP/3TC	1/27(3.7)		3/27(11.1)		0/22 (0.0)	
NVP/3TC/d4T	0/1(0.0)	0.458	0/1(0.0)	0.464	0/1(0.0)	0.872
Missing drug data	0/8(0.0)		0/8(0.0)		0/8(0.0)	

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Table 3.8 (Continued)

	n/N (%) with NRTI DRMs (N=275)	*P* value	n/N (%) with NNRTI DRMs (N=275)	*P* value	n/N (%) with PI DRMs (N=244)	*P* value
Maternal prophylaxis (PMTCT)						
No	4/101(4.0)		6/101(5.9)		1/90(1.1)	
Yes	9/162(5.6)	0.562	18/162(11.1)	0.157	3/142(2.1)	0.568
Missing data	1/12(8.3)		1/12(8.3)		0/12(0.0)	
AZT only	2/50(4.0)		5/50(10.0)		1/46(2.2)	
AZT/sdNVP	4/43(15.6)		5/43(11.6)		0/38(0.0)	
HAART	3/62(9.3)	0.554	7/62(22.5)	0.586	2/53(3.8)	0.482
Missing drug data	0/7(0.0)		1/7(14.3)		0/5(0.0)	
HIV-1 Subtype						
CRF01_AE	13/255(5.1)		24/255(9.4)		4/223(1.8)	
B	1/19(5.3)		1/19(5.3)		0/20(0.0)	
C	0/1(0.0)	0.973	0/1(0.0)	0.791	0/1(0.0)	0.826

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